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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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EXAMINER	ART UNIT	PAPER NUMBER
GAMBEL, P	1644	12

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DATE MAILED: 04/18/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 2/7/00

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 22, 23, 27, 29-45 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 22, 23, 27, 29-45 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

DETAILED ACTION

1. Applicant's amendment, filed 2/7/00 (Paper No. 11), is acknowledged.
Claims 1-21, 24-26 and 28 have been canceled.
Claims 22 and 23 have been amended.
Claims 29-45 have been added

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

Claims 22, 23, 27 and 29-45 are pending and under consideration.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 2/7/00 (Paper No. 11). The rejections of record can be found in the previous Office Action (Paper No. 8).

3. Applicant's request for clarification on Point 1 is rendered moot in view of applicant's canceled, amended and added claims; given that the instant claims are limited to L-selectin-specific antibodies.

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 8.

Applicant's amendment, filed 2/7/00 (Paper No. 11), states that 37 CFR 1.84 need not be complied with until allowance.

5. Claims 27, 40 and 44 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27, 40 and 44 are indefinite in the recitation of "Dreg 55 or HuDreg 55, HuDreg 200" because their characteristics are not known. The use of "these terms" as the sole means of identifying the claimed antibodies renders the claim indefinite because "these terms" are merely laboratory designations which do not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct cell lines or hybridomas. Applicant should amend the claims to include the SEQ ID NOS. to clearly identify the biological species.

Applicant's arguments and amended claims, filed 2/7/00 (Paper No. 11), have been fully considered but have not been found convincing. Applicant appears to rely upon the recitation of sequence information in the instant claims.

However, the Dreg 55, HuDreg 55, HuDreg 200 appears to read on the entire antibodies or humanized antibodies and not on variable regions of said antibodies as currently recited in the instant claims. No sequence has been recited for the entire Dreg 55 antibody. Therefore, applicant should amend the claims to include the SEQ ID NOS. to clearly identify the entire immunoglobulin species.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. MPEP 714.02 and 2163.06

6. Claims 22, 23, 27, 29-33, 39, 41-45 are rejected under 35 U.S.C. § 102(b) as being anticipated by Co (WO 94/12215) essentially for the reasons of record in previous Office Action (Paper No. 8).

Co teaches the use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Methods of Use). The Methods of Use set forth methods of administering and dosing, which encompass doses before, during and after the thrombolytic/emergency event, including repeated dosing at intervals that will depend upon the severity of the disease and general state of the patient's own immune system and at intervals to provide a quantity of the antibodies sufficient to effectively treat the patient (see pages 29-36; including page 29, paragraph 1; page 30, paragraphs 2-3; page 34, paragraph 3; , page 35, paragraphs 1-2). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies.

Applicant's arguments and amended claims, filed 2/7/00 (Paper No. 11), have been fully considered but have not been found convincing.

Applicant argues that standard for 35 USC 102 is not that no more of the reference is required than that it sets forth the substance of the invention but the standard is that all features of what is claimed must be taught explicitly and that the method itself must be taught.

Applicant argues that Co cites a number of possible approaches but does not mention polytrauma nor is there an suggestion which would suggest this.

Applicant relies upon pages 1-2 of the instant specification for a discussion on severe polytrauma.
Here, the specification as filed discloses that polytrauma is understood as an injury of a number of tissues (bones or soft tissue), which is associated with hemorrhagic shock and that multiple organ failure is a severe problem which occurs after polytrauma.

Applicant asserts that it is incorrect to think of the claimed invention as an aspect of the treatment of ischemic-reperfusion injury.

In contrast to applicant's assertions; page 4, paragraph 1 relies upon the art known association of the selections with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.
Applicant finds not mention in Co of heart/lung machines or any of the conditions elaborated in the claims.
Also, the specification as filed acknowledges the art known recognition that acute organ damage occurs after extracorporeal circulation during cardiovascular surgery such as bypass operation where the blood of the patient circulates extra corporeally through a heart-lung machine (e.g. see page 4, paragraph 4 of the specification)

In contrast to applicant's assertions, Co clearly teaches the use of L-selectin antibodies, including the use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic-reperfusion events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Methods of Use on pages 29-36). Therefore, Co does teach conditions such as multiple organ failure and ischemic-reperfusion events associated with cardiovascular surgery which read on the polytraumatic events encompassed by the claimed methods. Further, given the teachings of treating the ischemic-reperfusion events associated with cardiovascular surgery; the ordinary artisan at the time the time the invention was made would immediately envisage that such patients were on heart-lung machines as standard operating procedures. The prior art is employing the same reagents in the same patients to achieve the same end results as encompassed by the claimed methods.

In addition, applicant states that one cannot draw any conclusion as to extrapolating Co's work, as the art has noted failure in this regard (see LeukArrest fails in hemorrhagic shock); wherein the evidence suggests that the treatment of severe polytrauma especially multiple organ failure associated with L-selectin antibodies is not recommended.

However, it is noted that LeukArrest relies upon the CD11/CD18-specific 23F2G antibody specificity and not the L-selectin-specificity of the prior art and claimed methods.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant's arguments are not found persuasive.

7. Claims 29-33, 39, 41-45 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lefer (WO 95/95181) essentially for the reasons of record in previous Office Action (Paper No. 8).

Lefer teaches the use of humanized DREG 200 to inhibit a number of disorders or conditions encompassed by the claimed methods (e.g. ischemic events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods). The Therapeutic Methods forth methods of administering and dosing, which encompass doses before, during and after the ischemic-reperfusion events encompassing emergencies, including repeated dosing at intervals that will depend upon the severity of the disease and general state of the patient's own immune system and at intervals to provide a quantity of the antibodies sufficient to effectively treat the patient, including achieve optimal plasma levels of the antibody (see pages 21-26; including page 21, paragraph 3; page 23, paragraphs 2-3; page 25, paragraphs 2-3). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies.

Applicant's arguments and amended claims, filed 2/7/00 (Paper No. 11), have been fully considered but have not been found convincing.

Applicant arguments appear to be the same as that set forth above in Section 7 with respect to Co (WO 94/12215).

Applicant relies upon pages 1-2 of the instant specification for a discussion on severe polytrauma.
Here, the specification as filed discloses that polytrauma is understood as an injury of a number of tissues (bones or soft tissue), which is associated with hemorrhagic shock and that multiple organ failure is a severe problem which occurs after polytrauma.

Applicant asserts that it is incorrect to think of the claimed invention as an aspect of the treatment of ischemic-reperfusion injury.

In contrast to applicant's assertions; page 4, paragraph 1 relies upon the art known association of the selections with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.
Applicant finds no mention in Lefer of heart/lung machines or any of the conditions elaborated in the claims.
Also, the specification as filed acknowledges the art known recognition that acute organ damage occurs after extracorporeal circulation during cardiovascular surgery such as bypass operation where the blood of the patient circulates extra corporeally through a heart-lung machine (e.g. see page 4, paragraph 4 of the specification)

In contrast to applicant's assertions, Lefer clearly teaches the use of L-selectin antibodies, including the use of humanized DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic-reperfusion events, cardiac surgery, angioplasty, hemorrhagic shock) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods on pages 21-26). Therefore, Lefer does teach conditions such as hemorrhagic shock and ischemic-reperfusion events associated with cardiovascular surgery which read on the polytraumatic events encompassed by the claimed methods. Further, given the teachings of treating the ischemic-reperfusion events associated with cardiovascular surgery; the ordinary artisan at the time the time the invention was made would immediately envisage that such patients were on heart-lung machines as standard operating procedures. The prior art is employing the same reagents in the same patients to achieve the same end results as encompassed by the claimed methods.

In addition, applicant states that one cannot draw any conclusion as to extrapolating Lefer's work, as the art has noted failure in this regard (see LeukArrest fails in hemorrhagic shock); wherein the evidence suggests that the treatment of severe polytrauma especially multiple organ failure associated with L-selectin antibodies is not recommended.
However, it is noted that LeukArrest relies upon the CD11/CD18-specific 23F2G antibody specificity and not the L-selectin-specificity of the prior art and claimed methods.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant's arguments are not found persuasive.

8. Claims 29-33, 39, 41-45 are rejected under 35 U.S.C. § 102(e) as being anticipated by Tedder et al. (U.S. Patent No. 5,679,346) essentially for the reasons of record in previous Office Action (Paper No. 8).

Tedder et al. teaches the use of LAM-1-specific antibodies including recombinant antibodies thereof to inhibit a number of disorders or conditions encompassed by the claimed methods (e.g. neutrophil-mediated inflammation, reperfusion injury and multi-organ failure) (see entire document, including columns 6-7, overlapping paragraph). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with LAM-1-specific antibodies. The LAM-1 specificity is the same as the L-selectin specificity.

Applicant's arguments and amended claims, filed 2/7/00 (Paper No. 11), have been fully considered but have not been found convincing.

Applicant arguments are the same as that set forth above in Section 7 with respect to Co (WO 94/12215).

Applicant relies upon pages 1-2 of the instant specification for a discussion on severe polytrauma.
Here, the specification as filed discloses that polytrauma is understood as an injury of a number of tissues (bones or soft tissue), which is associated with hemorrhagic shock and that multiple organ failure is a severe problem which occurs after polytrauma.

Applicant asserts that it is incorrect to think of the claimed invention as an aspect of the treatment of ischemic-reperfusion injury.

In contrast to applicant's assertions; page 4, paragraph 1 relies upon the art known association of the selections with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.

In contrast to applicant's assertions, Tedder clearly teaches the use of L-selectin antibodies, including the use of recombinant/chimeric L-selectin antibodies to inhibit clinical manifestations encompassed by the claimed methods (e.g. reperfusion injury and multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly column 6, paragraph 4). Therefore, Tedder does teach conditions such as multiple organ failure and reperfusion injury encompassed by the claimed methods. The prior art is employing the same reagents in the same patients to achieve the same end results as encompassed by the claimed methods.

In addition, applicant states that one cannot draw any conclusion as to extrapolating Tedder's work, as the art has noted failure in this regard (see LeukArrest fails in hemorrhagic shock); wherein the evidence suggests that the treatment of severe polytrauma especially multiple organ failure associated with L-selectin antibodies is not recommended.
However, it is noted that LeukArrest relies upon the CD11/CD18-specific 23F2G antibody specificity and not the L-selectin-specificity of the prior art and claimed methods.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant's arguments are not found persuasive.

9. Claims 22, 23, 27 and 29-45 are rejected under 35 U.S.C. § 103 as being unpatentable over Co (WO 94/12215) AND/OR Lefer (WO 95/1515181) AND/OR Tedder et al. (U.S. Patent No.5,679,346 5,679) AND/OR Buerke et al. (J. Pharmacology and Experimental Therapeutics 271: 134-142, 1994) in view of Butcher et al. (U.S. Patent No. 5,316,913), Springer et al. (U.S. Patent No. 5,460,945), Moat et al. Ann. Thorac. Surg., 1993; 1449), Finn et al. (Perfusion, 1993)
essentially for the reasons of record in previous Office Action (Paper No. 8).

Applicant's arguments and amended claims, filed 2/7/00 (Paper No. 11), have been fully considered but have not been found convincing.

Applicant arguments are the same as that set forth above in Section 7 with respect to Co (WO 94/12215).
Applicant states the secondary references do no remedy the failings of the primary references.

In addition to the rejection of record ser forth in Paper No. 8; applicant's arguments and the examiner's rebuttal are essentially those set forth above in Sections 7-9.

While it is acknowledged that the prior art does not explicitly disclose polytraumatic events; it is clear that the prior art methods encompass polytraumatic events by teaching inhibiting multi organ failure and hemorrhagic shock with L-selectin antibodies.

The prior art clearly teaches ischemic-reperfusion events associated with cardiovascular surgery which read on the claimed methods. Further, given the teachings of treating the ischemic-reperfusion events associated with cardiovascular surgery; the ordinary artisan at the time the time the invention was made would immediately understand that such patients were on heart-lung machines as standard operating procedures.

The prior art is employing the same reagents in the same patients to achieve the same end results as encompassed by the claimed methods.

In addition as pointed out in the previous Office Action; Buerke et al. differs from the instant methods by not disclosing extracorporeal circulation and polytraumatic event per se, however in treating the reperfusion injury targeted by Buerke, it would have been obvious to treat similar conditions associated with extracorporeal circulation and traumatic events that would benefit from the inhibition of neutrophil-endothelial interactions.

In addition as pointed out in the previous Office Action; Springer et al. teaches the use of inhibitors of neutrophil-endothelial interactions such as L-selectin antagonists (column 13, lines 42-57) including targeting the therapeutic endpoints encompassed by the instant methods (see entire document, including column 30 Section 5.11).

In addition as pointed out in the previous Office Action; Moat et al. and Finn et al. teach the role of neutrophil adhesion and activation in cardiopulmonary bypass and the importance of blocking said function.

Co, Lefer, Buerke et al. and Tedder et al. differ from the instant claimed methods by not disclosing all of the time points for administering the inhibitory L-selectin antibodies, however dosages and administration would rely upon the needs of the patient and the nature of the intended therapeutic endpoint. Co and Lefer do teach single and multiple administrations sufficient to treat or at least partially arrest the disease and its complications; which would depend on the severity of the disease and general state of the of the immune system in a patient; which can be administered as bolus or repeated injections to achieve optimal plasma levels of antibody and alone or in combination with other therapeutic agents or drugs (see Methods of Use/Therapeutic Methods). Also, the ordinary artisan would have expected to reduce the probability of organ failure after a polytraumatic event, given the teachings of the prior art, including Methods of Use/Therapeutic Methods, as taught by Co and Lefer.

The prior art made and used L-selectin antibodies including the DREG 55 and DREG 200 specificities to inhibit inflammation including those associated with neutrophil adhesion and activation and the nature of the injuries claimed in the instant methods.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of L-selectin-specific antibodies as a therapeutic regimen in treating cardiovascular and traumatic diseases. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PhilipGambel

Phillip Gambel, PhD.
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April 17, 2000